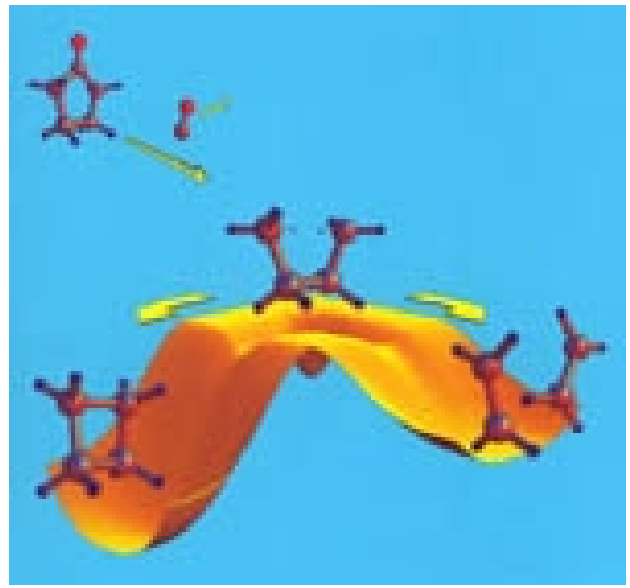
Review

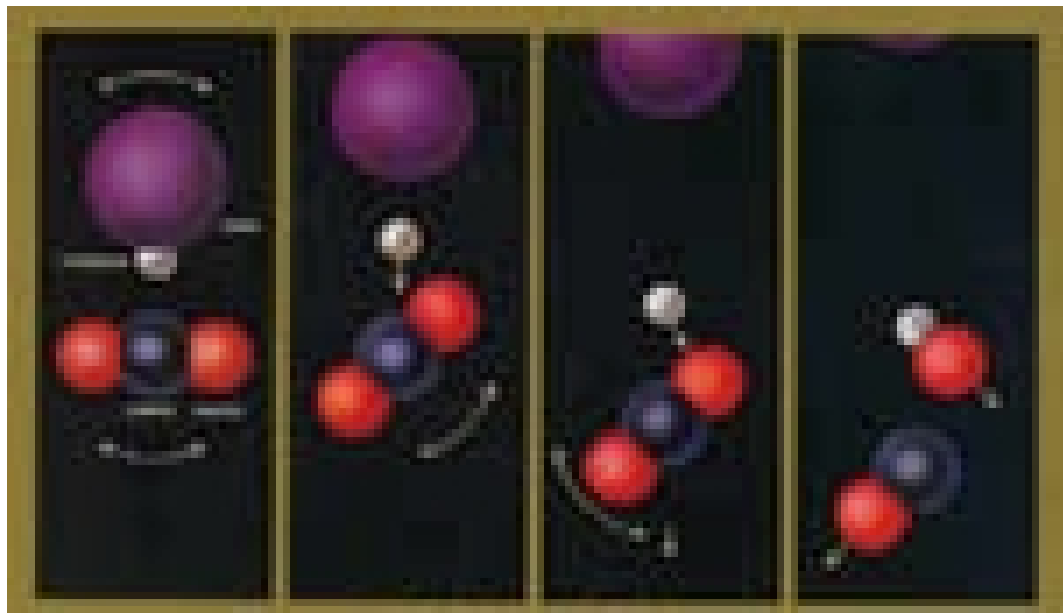
Remember: Next Exam Date– ***Wednesday, April 4th!***

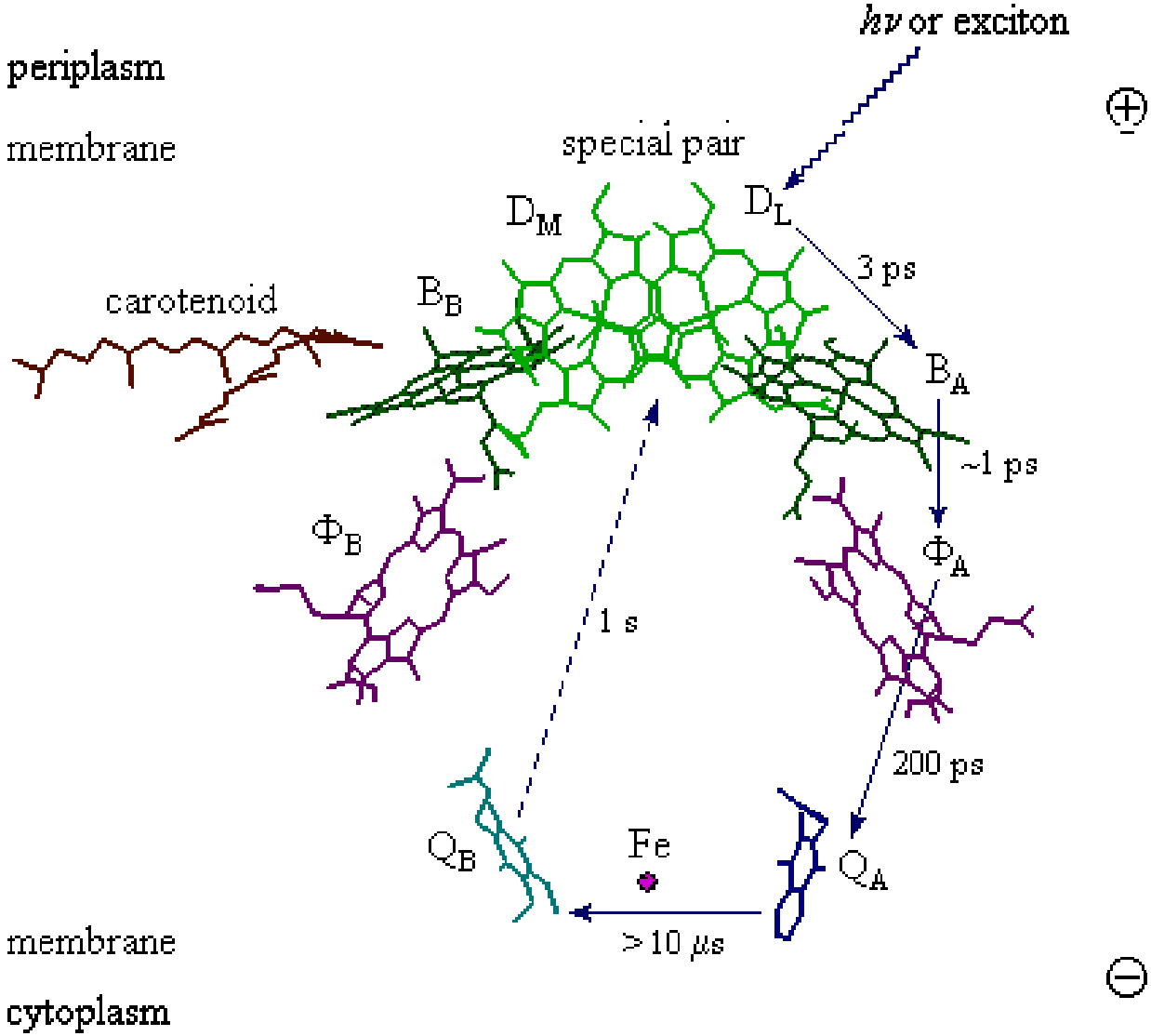
A review of free energy, equilibrium constants, and electrochemistry

Ahmed Zewail
1999 Nobel Prize in Chemistry

Femtochemistry
Femtobiology






hν or exciton
periplasm
membrane
special pair
D_M
D_L
3 ps
carotenoid
B_B
B_A
~1 ps
Φ_B
Φ_A
1 s
200 ps
Q_B
Fe
Q_A
> 10 μs
membrane
cytoplasm

The Nernst Equation

Because these electrochemical reactions are so important to cellular function and the ***measurement*** of cellular function let's examine

$$\Delta G\ (J) = -n\ F\ \mathcal{E}$$

in greater detail.

Using another relation for ΔG

$$\Delta G = -n\ F\ \mathcal{E} = \Delta G^\circ + RT\ \ln(Q)$$

Now,

$$\Delta G^\circ = -RT\ \ln(K) = -n\ F\ \mathcal{E}^\circ$$

So

$$-n\ F\ \mathcal{E} = -n\ F\ \mathcal{E}^\circ + RT\ \ln(Q)$$

$$\mathcal{E} = \mathcal{E}^\circ - RT\ \ln(Q)/n\ F \quad \text{(Nernst Equation)}$$

$$\mathcal{E} = \mathcal{E}^\circ - 0.059 * \log(Q)/n \quad \text{(at 298K)}$$

The reduction potential is intensive!

		ε° (volts)
	0.5 Pyruvate + H^+ + e^- ⟶ 0.5 lactate	-0.19
−	0.5 NAD^+ + 0.5 H^+ + e^- ⟶ 0.5 NADH	-0.32
	0.5 (Pyruvate + H^+ + NADH ⟶ lactate + NAD^+)	0.13

The standard reduction potential doesn't change because all the stoichiometry gets balanced in the Nernst equation.

$$\varepsilon^\circ = \frac{RT}{n\Im}\ln(K) = \frac{RT}{1*\Im}\ln\left(\frac{a_{lactate}^{1/2}a_{NAD^+}^{1/2}}{a_{pyruvate}^{1/2}a_{H^+}^{1/2}a_{NADH}^{1/2}}\right) = \frac{RT}{2*\Im}\ln\left(\frac{a_{lactate}a_{NAD^+}}{a_{pyruvate}a_{H^+}a_{NADH}}\right)$$

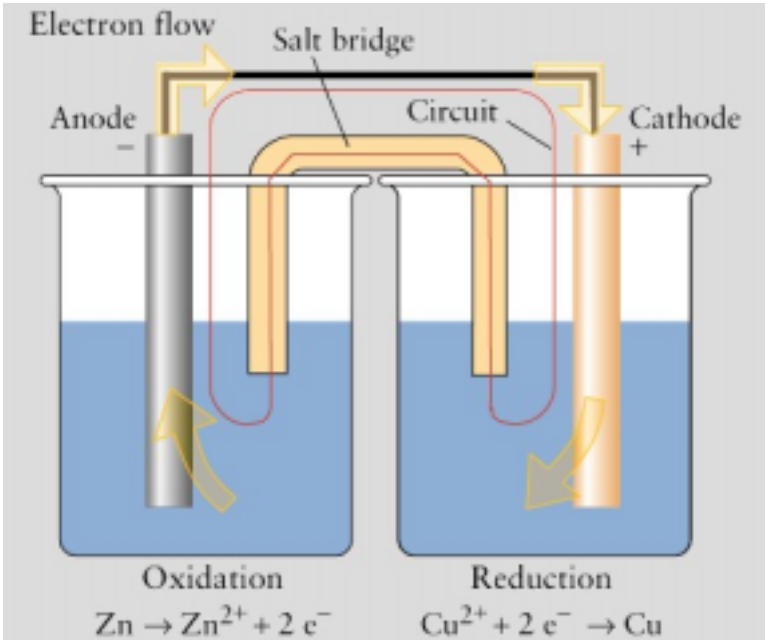
That is, the electrochemical potential is an intensive property, i.e. it is measured on a per mole basis!

The Standard Electrode and Half-Cells

We found that the standard electrode potential $\mathcal{E}^\circ$ can be measured and tabulated as half-cell potentials.

Half-cells are really defined as pure oxidation or reduction reactions.

We really can't have an oxidation without a reduction reaction and *vice versa*.



We can formally write these separate half-reactions and measure a standard potential for them.

But, of course, we must have a standard reference. This is the hydrogen electrode:

$$2\,H^+ + e^- \longrightarrow H_2(g) \qquad \mathcal{E}^\circ = 0.0 \text{ @ pH=0.0}$$

Table 4.4 Standard reduction electrode potentials at 25°C

Oxidant/Reductant	Electrode reaction	$\mathscr{E}^0$ (V)*	$\mathscr{E}^{0\prime}$ (V)† (pH 7)
Li^+/Li	$Li^+ + e^- \rightarrow Li$	−3.045	
Na^+/Na	$Na^+ + e^- \rightarrow Na$	−2.714	
Mg^{2+}/Mg	$Mg^{2+} + 2e^- \rightarrow Mg$	−2.363	
$OH^-/H_2/Pt$	$2H_2O + 2e^- \rightarrow H_2 + 2OH^-$	−0.8281	
Zn^{2+}/Zn	$Zn^{2+} + 2e^- \rightarrow Zn$	−0.7628	
Acetate/acetaldehyde	$OAc^- + 3H^+ + 2e^- \rightarrow CH_3CHO + H_2O$		−0.581
Fe^{2+}/Fe	$Fe^{2+} + 2e^- \rightarrow Fe$	−0.4402	
Gluconate/glucose	$C_6H_{11}O_7^- + 3H^+ + 2e^- \rightarrow C_6H_{12}O_6 + H_2O$		−0.44
Spinach ferredoxin	$Fd[Fe(III)] + e^- \rightarrow Fd[Fe(II)]$		−0.432
CO_2/formate	$CO_2 + 2H^+ + 2e^- \rightarrow HCO_2^- + H^+$	−0.20	−0.42
$NAD^+/NADH$‡	$NAD^+ + H^+ + 2e^- \rightarrow NADH$	−0.105	−0.320
Fe^{3+}/Fe	$Fe^{3+} + 3e^- \rightarrow Fe$	−0.036	
$H^+/H_2/Pt$	$2H^+ + 2e^- \rightarrow H_2$	0	−0.421
Acetoacetate/ β-hydroxybutyrate	$CH_3COCH_2CO_2^- + 2H^+ + 2e^- \rightarrow CH_3CHOHCH_2CO_2^-$		−0.346
Mn hematoporphyrin IX	$He[Mn(III)] + e^- \rightarrow He[Mn(II)]$		−0.342
$NADP^+$/NADPH	$NADP^+ + H^+ + 2e^- \rightarrow NADPH$		−0.324
Horseradish peroxidase	$HRP[Fe(III)] + e^- \rightarrow HRP[Fe(II)]$		−0.271
FAD/$FADH_2$§	$FAD + 2H^+ + 2e^- \rightarrow FADH_2$		−0.219
Acetaldehyde/ethanol	$CH_3CHO + 2H^+ + 2e^- \rightarrow CH_3CH_2OH$		−0.197
Pyruvate/lactate	$CH_3COCO_2^- + 2H^+ + 2e^- \rightarrow CH_3CHOHCO_2^-$		−0.18
Oxaloacetate/malate	$^-O_2CCOCH_2CO_2^- + 2H^+ + 2e^- \rightarrow {}^-O_2CCHOHCH_2CO_2^-$		−0.166
Fumarate/succinate	$^-O_2CCH{=}CHCO_2^- + 2H^+ + 2e^- \rightarrow {}^-O_2CCH_2CH_2CO_2^-$		+0.031
Myoglobin	$Mb[Fe(III)] + e^- \rightarrow Mb[Fe(II)]$		+0.046
Dehydroascorbate/ ascorbate	$C_6H_7O_7^- + 2H^+ + 2e^- \rightarrow C_6H_9O_7^-$		+0.058
Ubiquinone	$UQ + 2H^+ + 2e^- \rightarrow UQH_2$		+0.10
$AgCl/Ag/Cl^-$	$AgCl + e^- \rightarrow Ag + Cl^-$	+0.2223	
Calomel	$\frac{1}{2}Hg_2Cl_2 + e^- \rightarrow Hg + Cl^-$	+0.268	
Cytochrome *c*	$Cyt[Fe(III)] + e^- \rightarrow Cyt[Fe(II)]$		+0.254
Cu^{2+}/Cu	$Cu^{2+} + 2e^- \rightarrow Cu$	+0.337	
$I_2/I^-/Pt$	$I_2 + 2e^- \rightarrow 2I^-$	+0.5355	
$O_2/H_2O_2/Pt$	$O_2 + 2H^+ + 2e^- \rightarrow H_2O_2$	+0.69	+0.295
$Fe^{3+}/Fe^{2+}/Pt$	$Fe^{3+} + e^- \rightarrow Fe^{2+}$	+0.771	
Ag^+/Ag	$Ag^+ + e^- \rightarrow Ag$	+0.799	
$NO_3^-/NO_2^-/Pt$	$NO_3^- + 2H^+ + 2e^- \rightarrow NO_2^- + H_2O$	+0.94	+0.421
$Br_2/Br^-/Pt$	$Br_2 + 2e^- \rightarrow 2Br^-$	+1.087	
$O_2/H_2O/Pt$	$O_2 + 4H^+ + 4e^- \rightarrow 2H_2O$	+1.229	+0.816
$Cl_2/Cl^-/Pt$	$Cl_2 + 2e^- \rightarrow 2Cl^-$	+1.359	
$Mn^{3+}/Mn^{2+}/Pt$	$Mn^{3+} + e^- \rightarrow Mn^{2+}$	+1.4	
$Ce^{4+}/Ce^{3+}/Pt$	$Ce^{4+} + e^- \rightarrow Ce^{3+}$	+1.61	
$F_2/F^-/Pt$	$F_2 + 2e^- \rightarrow 2F^-$	+2.87	

* $\mathscr{E}^0$ refers to the solute standard state with unit activity for all species.
† $\mathscr{E}^{0\prime}$ refers to the biochemist's standard state with pH 7.
‡ NAD^+ is nicotinamide adenine dinucleotide.
§ FAD is flavin adenine dinucleotide.

The Nernst Equation and Redox Buffers

Redox buffers are much the same as pH buffers.

They resist changes in potential after small additions of reductants or oxidants.

They have a buffering capacity that is maximized when the concentrations of both oxidized and reduced forms of the buffer are high

Let's say we wish to make a buffer of with NADH

					$\varepsilon^{\circ\prime}$ (volts)
NAD^+	+	$H^+ + 2\ e^-$	$\longrightarrow$	NADH	-0.32

Which means it's a worse oxidizing agent than H^+ at pH 0.0.
But this isn't pH 0.0! We're at pH 7.0!

$$\varepsilon^{\circ'} = \varepsilon^{\circ} - \frac{0.059}{2}\log\left(\frac{P_{H_2(g)}}{a^2_{H^+}}\right) = -0.421V$$

$P_{H2\,(g)}$= 1 atm
a_{H+}= 1 @ pH 0.0
a_{H+}= 10^{-7} @ pH 7.0

So we've found that (for the reactions in the reverse direction)

$\varepsilon^{\circ\prime}$(oxidation)= 0.32 V for the NADH oxidation

and

$\varepsilon^{\circ\prime}$ (oxidation)= 0.421 V for the H_2 oxidation

So under these conditions H_2 is a *better* reducing agent that NADH at pH 7.0!

At pH 0.0 we find ε°(oxidation) for the NADH oxidation reaction is 0.105.

Under these conditions NADH is the better reducing agent!

Why does the order change with pH? What the implications for cell function?

Redox Buffers and Disulfide Bonds

Cells use Redox Buffers to detect large changes in the reduction potential of the cell. This potential changes, for example, with the amount of oxygen in the cell.

Fermentations are done anaerobically, i.e. is a more reducing environment
Respiration is done aerobically, i.e. is a more oxidizing environment.

When making wine from grapes we ferment the grapes.

What happens when we let oxygen in?

The two different outcomes aren't only due to the passive oxidative properties of oxygen. The yeast *respond* directly to changes in oxygen level to change the activities of proteins.

One major player in sensing these levels is **glutathione**= Glu-Cys-Gly
Which can undergo the following reaction:

$$2\ G\text{-}SH \longleftarrow G\text{-}S\text{-}S\text{-}G + 2\ H^+ + 2\ e^- \qquad \varepsilon^{\circ\prime} = -0.26V$$

So comparing glutathione reduction to NAD^+

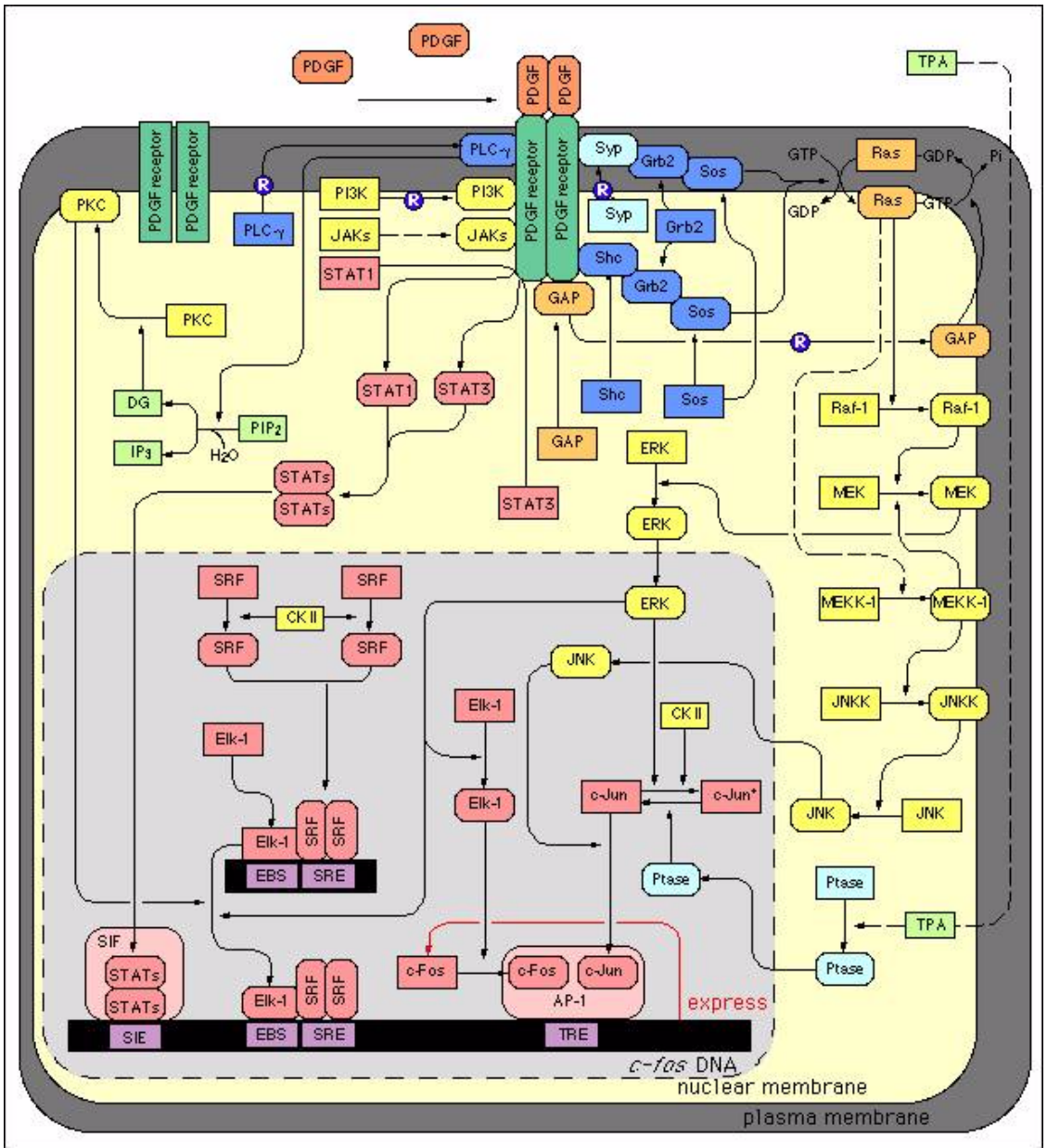
		$\varepsilon^{\circ\prime}$ (volts)
$NAD^+ + H^+ + 2\ e^-$	$NADH$	-0.32
$G\text{-}S\text{-}S\text{-}G + 2\ H^+ + 2\ e^-$	$2\ G\text{-}SH$	-0.26

we find that if we have both NAD^+ and glutathione around, then depending on their concentrations one will reduce the other.

If we have roughly equal amounts of NAD^+ and NADH and amounts of G-SH and and G-S-S-H such that K=1, then G-S-S-H will oxidize NADH until the two electrical potentials are equal.

You should know how to calculate this!

Platelet-Derived Growth Factor Pathway.



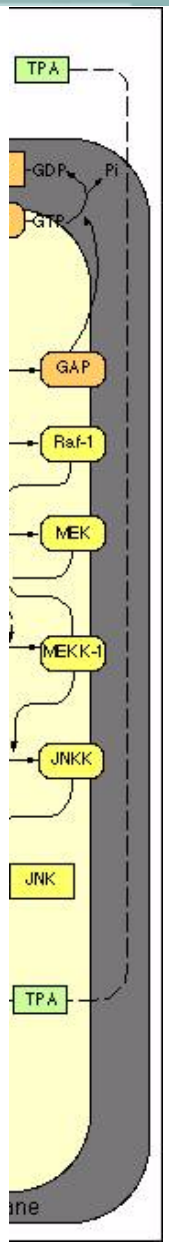
Now if we really want to understand cellular function we've left out a lot of important chemistry and physics so far.

We will rectify this partly in the next few weeks.

The natural next step is physical equilibria.

Membranes and Transport
Ligand Binding
Colligative Properties

Membranes and Transport

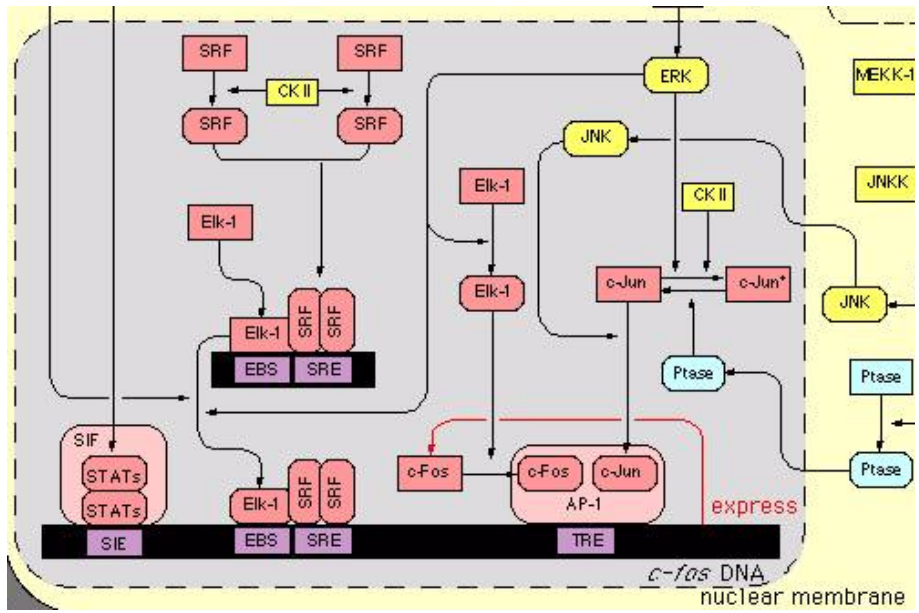


Cells separate themselves from the surroundings by membranes. They also use membrane compartments to separate chemical processes, to store excess materials, and to move things about.

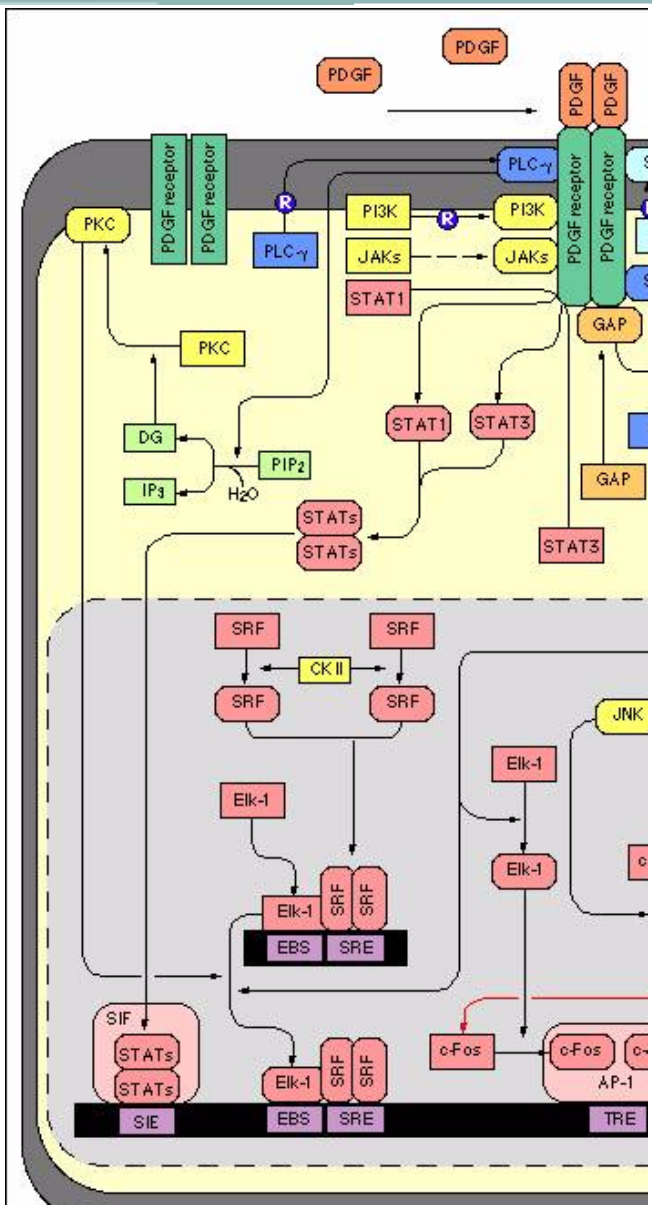
These membranes are generally a bilayer. Often only 2 molecules thick.

Not only are these membranes a separate phase from the cytoplasm or the periplasm but they can themselves fragment into different lipid phases.

Each of these phases exists based on different surface potentials, temperature, pressure, local stress, electrical potential.



Ligand Binding



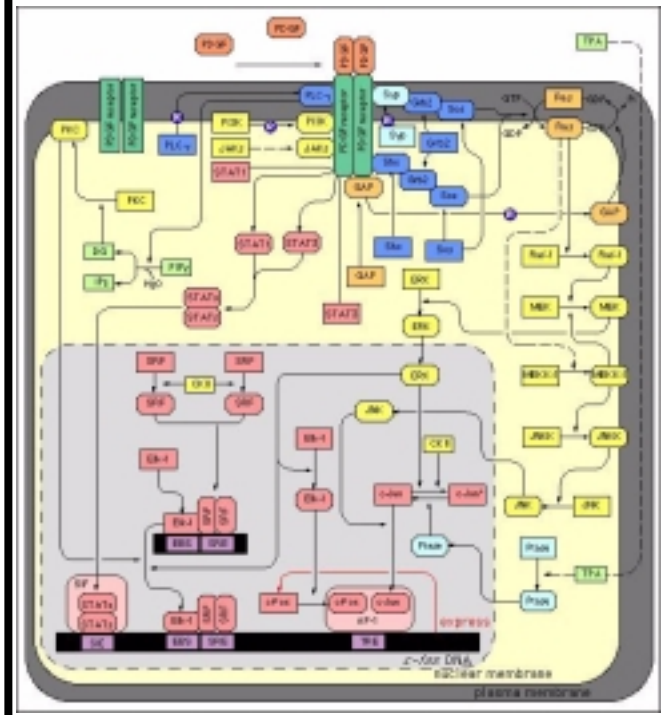
Well, we have dealt with this before but we haven't dealt with what happens when different phases or compartments are involved!

Look at the STAT proteins. These can only get transported to the nucleus in dimer form.

How does this affect it partitioning assuming, of course, that there is no active transport. (There is.)

How does the binding of the dimer to the DNA affect this transport?

Colligative Properties



These are properties that depend only on the number of particles in solution and not their nature.

For an ideal gas: Pressure is a colligative property.

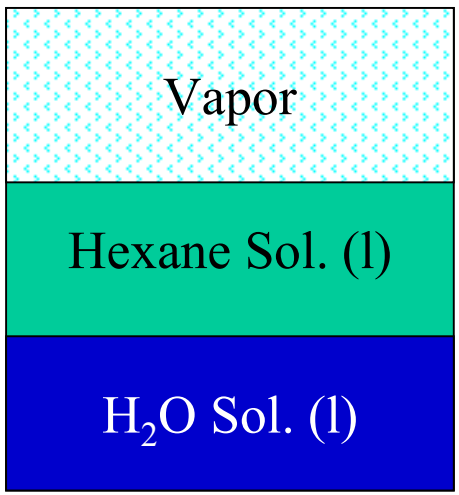
In solution we will find that boiling and freezing points show colligative properties.

Phase Equilibria

What happens when you try and get a hydrophilic drug across a cell membrane?

In general, unless there is a specific active transport process, it is very difficult. But you can always get some in since there is usually some partition between phases.

Let's consider a simple system composed of H_2O, Hexane in both liquid and gas form.



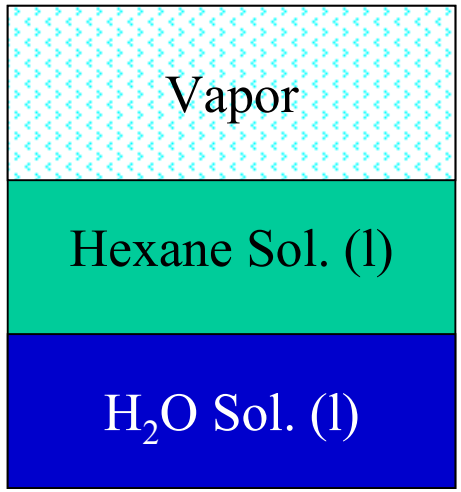
If we wait long enough this system will come to equilibrium.

We find that there is

some hexane in the water.
some water in the hexane
a mixture of water and hexane gas.

We know that the chemical potentials for each species in all phases of this system are equal.

Phase Equilibria



If we use the same standard state for all phases then the fact that

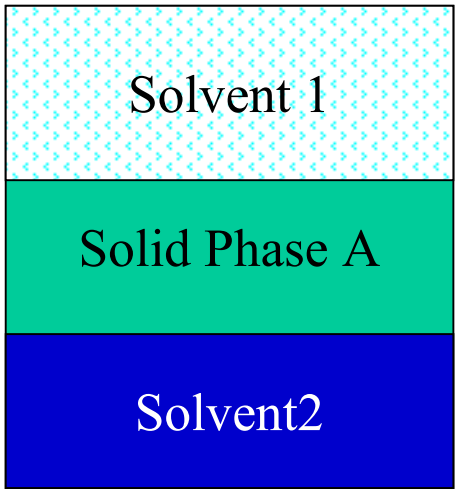
$$\mu_{\text{hexane (l)}} = \mu_{\text{hexane (aq)}} = \mu_{\text{hexane (g)}}$$

implies that the activity of hexane in all three phases is the same.

But we know the concentrations are different!

So what's different?

Phase Equilibria



Now what?

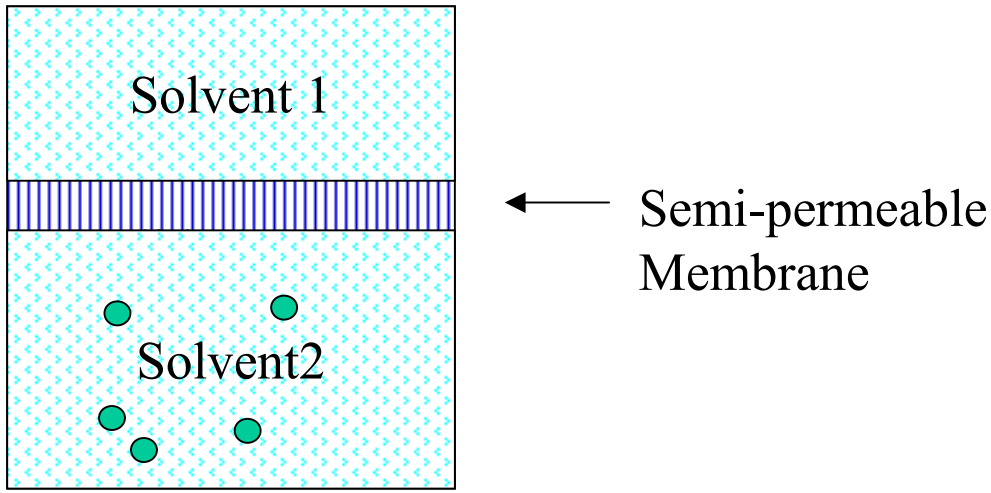
Well, if we let it come to equilibrium and assume that there is a vast excess of the solid phase then we know something strange:

$$\mu_{A\ (solvent\ 1)} = \mu_{A\ (solvent\ 2)} = \mu_{A\ (solid)}$$

So we can directly calculate the $\Delta\mu$ for transferring A from one solvent to the other, right?

We measure the activity of our solute in the two phases and since the μ°'s are different for the two solute standard states (which have a solute activity of 1), we can calculate this difference by plugging in our measurements.

What happens in this case?



● = a protein that can bind a solute dissolved in the solvents

Homework:

Reading: Chapter 5

TSW 5.2, 5.3(a), 5.5, 5.6, 5.7, 5.9